

calcium thereto.--

Replace the paragraph beginning at page 10, line 1, with the following rewritten paragraph:

--(ii) A peptide consisting of the amino acid sequence 1-114 of (SEQ ID NOS 2 and 4) of the Sequence Table and binding calcium thereto.--

Replace the paragraph beginning at page 10, line 4, with the following rewritten paragraph:

--(iii) A peptide having an amino acid sequence in which one or more amino acids are deleted from or added to the amino acid sequence of (SEQ ID NOS 3 or 4) of the Sequence Table, or one or more amino acids in the amino acid sequence of (SEQ ID NOS 3 or 4) are replaced with other amino acids, binding calcium thereto, and exhibiting the activity of increasing secretion of granules of cell lines having granule secretion capability.--

Replace the paragraph beginning at page 16, line 5, with the following rewritten paragraph:

--As a method of causing calgranulin to over-expression, a method of recombining a gene encoding calgranulin in a known plasmid vector or virus vector, and introducing the recombinant into the cells can be given. The base sequence shown as (SEQ ID NOS 1 or 2) in the sequence table, for example, can be used as a gene encoding calgranulin. The recombinant vector can be introduced into the cells by the calcium phosphate method, the DEAE dextran method, lipofectin method, electric pulse method, or the like. The above-described various methods may be preferably used for introducing a calgranulin gene in a cell line and causing the calgranulin to over-expression. The cells are

converted to cells having the above-mentioned permeabilized cell membrane and a water-soluble calcium compound is preferably introduced in the cell line. Specifically, a calgranulin gene is introduced into cells by incubating a plasmid vector or virus vector in which the calgranulin gene has been incorporated in the amount of the 1-200  $\mu$ g per  $0.5 \times 10^7$  to  $3 \times 10^7$  cells at 4-40°C for 5-120 minutes together with 1-100  $\mu$ g of calcium phosphate, 0.1-10 mg of DEAE dextran, or 1-100  $\mu$ g of lipofectin, or by treating the plasmid vector or virus vector in which the calgranulin gene has been incorporated in the amount of the 1-200  $\mu$ g per  $0.5 \times 10^7$  to  $3 \times 10^7$  cells using a short electric pulse at 4-40°C for 1-30 minutes. The above-mentioned various methods may be used for introducing the water-soluble calcium compound.--

Replace the paragraph beginning on page 19, line 1, with the following rewritten paragraph:

--A calgranulin anti-sense gene can be obtained by inserting a gene having a base sequence complementary to the base sequence shown by (SEQ ID NOS 1 or 2), for example. In the present invention, a plasmid vector or virus vector is prepared by inserting 1-200  $\mu$ g of this calgranulin anti-sense gene per  $0.5 \times 10^7$  to  $3 \times 10^7$  cells. The resulting vector is incubated at 4-40°C for 5-120 minutes with the addition of 1-100  $\mu$ g of calcium phosphate, 0.1-10 mg of DEAE dextran, or 1-100  $\mu$ g of lipofectin. Alternatively, a plasmid vector or virus vector with 1-200  $\mu$ g of the calgranulin anti-sense gene inserted per  $0.5 \times 10^7$  to  $3 \times 10^7$  cells is added and treated by a short electric pulse at 0.05-0.5 kV at a temperature of 4-40°C for 1-30 minutes.--